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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,787	07/30/2007	Kazuhiro Nagaike	59150-8037	3253

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King & Spalding LLP
P.O. Box 889
Belmont, CA 94002-0889

EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
04/13/2012	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,787	NAGAIKE ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2012*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1,5,8-10,12-29,31-40,44-49,51-56,58-62,66-86 and 88-91* is/are pending in the application.

5a) Of the above claim(s) *5,19-29,31-40,44-49,51-56,58-62,66-86 and 88-91* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,8-10 and 12-18* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *05 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/19/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's submission filed on March 28, 2012 has been entered. Claims 1, 8-10 and 12-18 are under examination. All other pending claims are withdrawn from consideration being drawn to non-elected subject matter.

Response to Amendment

2. The rejection of claims 1, 8-10 and 12-18 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of Applicant's amendment.

Claims Summary

3. The claims are drawn to a recombinant varicella-zoster virus (VZV), also known as human herpes virus type 3, HHV-3, comprising a bacterial artificial chromosome (BAC) vector sequence that is inserted into a non-essential region of a VZV genome. The insertion is in the ORF of gene 13, a non-essential gene. Note that "the region in the ORF of gene 13" is the elected species; see the remarks filed by Applicant on March 3, 2009.

Also claimed are pharmaceutical compositions and vaccines containing the recombinant VZV. The BAC vector sequence comprises a recombinant protein dependent recombinant sequences, selected from the group consisting of a loxP site, an FRT site, an attB, an attP site and a res site. The BAC vector comprises a selectable marker (*e.g.*, drug selectable marker, or GFP). In one embodiment, the BAC vector comprises SEQ ID NO: 7. The VZV genome is comprises sequences from a wild type strain, an Oka vaccine strain, or a mutant type strain. The genome has mutations in gene 62 (*e.g.*, substitution at position 2210 to G, 3100 to G, 3818 to C, 4006 to G).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 8-10 and 12-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horsburgh *et al.* (US Patent 6,277,621 B1, "Horsburgh") in view of Cohen *et al.* (PNAS USA, 1993, 90:7376-7380, "Cohen") and Mori *et al.* (US Patent Application Publication 20080226677, filed May 12, 2004, "Mori").

Horsburgh discloses a recombinant VZV virus comprising a BAC vector sequence (see col. 6, lines 1-17, col. 1, lines 50-54, 65-67; col. 3, lines 41-48; and col.10, lines 15-18). The encoded virus is attenuated (see col. 2, lines 2-9). The BAC is inserted into a non-essential region of the virus genome (see col. 6, lines 40-54). Selectable markers, such as drugs and GFP are suggested (see col. 11, lines 18-29; and col. 12, line 67). Horsburgh suggests that the expression system can be used to generate attenuated or mutated viruses for purposes of immunization (see col. 5, lines 4-30).

Claims 11 and 12 require the presence of sequences from a wild type strain of VZV or a mutant type strain of VZV. The claims language indicates that only some sequences from the viral strains need be present. Since there are no particular sequences identified that must be included in the VZV genomes, it is reasonable to expect that any VZV genome will meet the limitations of these claims.

Although Horsburgh does not specifically suggest that the viruses be used as pharmaceutical compositions or vaccines, note that there are no additional components to render the actual contents of the composition distinct from a composition comprising the virus. Horsburgh's viruses are expected to be in some sort of culture or medium during their production and storage, which qualifies as a composition. Although the claims call the composition "pharmaceutical compositions" and "vaccines", the only contents of those compositions are the viruses, which is what Horsburgh teaches.

Horsburgh teaches that the BAC is inserted into a non-essential region of the virus genome (see col. 6, lines 40-54), but does not indicate which non-essential region. One of ordinary skill in the art would have been motivated to use any known non-essential region of VZV to insert the BAC, such as the ORF of gene 13, thymidylate synthetase. Cohen discloses that the VZV thymidylate synthetase (ORF of gene 13) is not essential for replication and is therefore non-essential (see abstract). One would have had a reasonable expectation of success in view of Cohen's recovery of virus particles.

Regarding the presence of a recombinant protein dependent recombinant sequence, Mori discloses the use of BAC vectors to express viral genes, as well as the use of recombinant protein dependent recombinant sequences as instantly claimed (see paragraph [0102] on page 8, and paragraph [0209] on page 26, for example). One would have been motivated to use such sequences in order to control the site of recombination. With regard to the BAC vector sequence comprising SEQ ID NO: 7, although Horsburgh does not disclose this particular sequence, it would have been obvious to have used any other available BAC vector sequence, such as the sequence taught by Mori as SEQ ID NO: 401 (100% identical to Applicant's SEQ ID NO: 7).

One would have had a reasonable expectation of success because Mori uses human herpesviruses (types 6 and 7) with the BAC vector sequence.

Regarding the particular strain and particular mutations embodied in claims 13-15, Horsburgh does not disclose these limitations. However, these mutations are attenuating mutations of a VZV Oka strain, as disclosed by Cohen. Cohen discloses particular mutations in gene 62 of VZV Oka strain that render the strain attenuated and useful as a vaccine. Given that Horsburgh suggests that genomes of live, attenuated viruses can be expressed from the BAC construct, it would have been obvious to have used the Oka strain with its attenuating mutations with a reasonable expectation of success because of its known attenuation and use as a live, attenuated virus vaccine (see Cohen, abstract).

Applicant's arguments have been carefully considered but fail to persuade. In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that the invention identifies a region where many non-essential genes are present and that region was appropriate for inserting BAC vector such that disruption of the function of the region is avoided. Applicant argues that the result was not expected and would not have been obvious. In response to Applicant's argument, the Office notes that Applicant has pointed out any evidence to suggest that the combination of teachings of the prior art would not have had a reasonable expectation of success. Applicant asserts that no reasoning has been provided for how or why the skilled artisan would have arrived at the claimed invention. In

response, the obviousness rejection does indeed address the reasoning. Applicant has not pointed out what exactly is deficient in the obviousness analysis.

In response to Applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 8-10 and 12-18 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 11-17, 24 and 25 of copending Application No. 12/094,757. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed subject matter of the co-pending application falls within the scope of the recombinant BAC instantly claimed. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. In the remarks filed March 28, 2012, Applicant requests that this provisional rejection be held in abeyance until allowable subject matter is indicated.

Applicant also remarks that it is improper for the Office to maintain a provisional obviousness-type double patenting rejection based on claims that have not been allowed or issued in a patent. In response to Applicant's remarks, it is proper for the Office to maintain a provisional rejection because the claims of either case have not been allowed or patented; this is the nature of the rejection being "provisional". As the instant claims are still rejected for other reasons besides the provisional rejection, the provisional rejection stands because there is no allowable subject matter.

Conclusion

6. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACY CHEN whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30), alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/
Primary Examiner, Art Unit 1648